IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Howard Bernstein, Donald Chickering, Sarwat Khattak, and Julie Straub

Serial No.: 09/731,412 Art Unit: 1617

Filed: December 6, 2000 Examiner: E.J. Webman

For: *MATRICES FORMED OF POLYMER AND HYDROPHOBIC COMPOUNDS FOR USE IN DRUG DELIVERY*

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY BRIEF

Sir:

This is a Brief in reply to the Examiner's Answer mailed December 24, 2002 in the above-identified patent application. A Request for Oral Hearing accompanies this Reply along with the fee for a small entity. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to 50-1868.

Appellants have appealed the final rejection of claims 20-24, and 27-32 in the Office Action mailed May 28, 2002 in the above-identified patent application. A Notice of Appeal was faxed on June 27, 2002. An Appeal Brief was mailed on September 6, 2002. An Examiner's Answer was mailed on December 24, 2002.

(1) REAL PARTY IN INTEREST

The real party in interest is set forth in the Appeal Brief.

(2) RELATED APPEALS AND INTERFERENCES

The related appeals are set forth in the Appeal Brief.

(3) STATUS OF CLAIMS ON APPEAL

Claims 20-34 are pending. Claims 20-24 and 27-32 are on appeal. Claims 25, 26, 33 and 34 are objected to. The text of each claim as pending is set forth in the Appendix to the Appeal Brief.

(4) STATUS OF AMENDMENTS

The status of amendments is set forth in the Appeal Brief.

(5) SUMMARY OF THE INVENTION

The summary of the invention is set forth in the Appeal Brief.

(6) ISSUE ON APPEAL

The issue presented on appeal is set forth in the Appeal Brief.

(7) GROUPING OF CLAIMS

The grouping of claims is set forth in the Appeal Brief.

(8) ARGUMENTS

Appellants affirm all of the arguments made in the Appeal Brief.

Gombotz is directed at solving a completely different problem than the problem that is solved by the present application. Gombotz discloses matrices resulting in *prolonged*, controlled release of GM-CSF (abstract and col. 2, lines 16-17). In contrast, Appellants' claims are directed at methods for administering drug in matrices with rapid release of drug from the matrix (see claim 20). Gombotz teaches that the drug is released for at least six to seven days (col. 4, lines

15-17) and provides *in vitro* data demonstrating linear release for six days (see Figures 1b, 3a, and 4). By the *second day* of *in vitro* testing, *not even 50%* of the GM-CSF had been released (*see e.g.* Figures 1b and 3a). In contrast, the data in Howard Bernstein's declaration (herein referred to as "the Declaration"), which was submitted to the U.S.P.T.O. on February 22, 2002, demonstrates that the claimed matrices release *over 50%* of the agent, prednisone, in *two hours* (see Figure, Exhibit C). Further, Appellants' methods require that the "drug is released over shorter periods of time as compared to release from matrices not incorporating the hydrophobic or amphiphilic compound." (Claim 20) Therefore Gombotz's microparticles could not be used to practice the claimed methods.

The differences between the properties of Gombotz's microparticles and Appellants' are as a result of the method by which the matrices are formed. Gombotz does not require the inclusion of a pore forming agent and a hydrophobic or amphiphilic compound, while this is required in Appellants' method. As depicted in the Figure in the Declaration, the inclusion of both the pore forming agent and the hydrophobic or amphiphilic compound during the manufacturing process is critical to the production of a matrix with the desired quick release properties. (see also Appeal Brief, page 8, second paragraph)

The Examiner has mischaracterized the teachings of Gombotz. Gombotz does not teach or suggest the claimed methods for administering a therapeutic or prophylactic agent. The claimed methods require a matrix that is formed when (1) a hydrophobic or amphiphilic compound, the therapeutic or prophylactic agent to be incorporated, and a pore forming agent are

emulsified in a polymer solution and (2) the solvent and pore forming agent are removed in a single step. However, Gombotz does not teach either of these steps and forms a different matrix.

Gombotz contains a section which discusses different additives that can be added to the microparticles (see col. 9, line 31 until col. 10, line 8). Each paragraph of this section discusses a different type of excipient. The first paragraph of this section discusses the inclusion of acid and basic excipients to modify the degradation of the polymer (see col. 9, lines 32-35). These excipients are added to alter the polymer erosion rate. In this paragraph, Gombotz states that "the excipients can be mixed with the incorporated GM-CSF or can be dissolved within the polymer." (col. 9, lines 34-36) Thus, this statement refers to the acidic and basic excipients which were mentioned in the previous sentence.

Two paragraphs later, Gombotz discusses pore forming agents, which are defined as "water soluble compounds such as inorganic salts or sugars". (col. 9, lines 52-54) Gombotz does not teach nor suggest that the pore forming agents are the same as the acidic and basic excipients that were discussed in the first paragraph of this section. Thus, the organization of the text conflicts with the Examiner's interpretation at page 3 of the Examiner's Answer.

Gombotz teaches the formation of microparticles with slow release properties, which do not meet the requirements for the types of matrices that are administered in the claimed methods. Thus, Gombotz does not teach the claimed methods for administering a therapeutic or prophylactic agent. Therefore, claims 20-24 and 27-32 are novel over Gombotz.

The Board's attention is also drawn to the fact that the parent application, claiming the matrices *per se*, were allowed by this same examiner and have now issued as U.S. Patent No.

6,423,345. This patent was allowed over the same art cited against the claims to the method of use of the matrix here on appeal.

(9) SUMMARY AND CONCLUSION

For the foregoing reasons and those in the Appeal Brief, Appellant submits that claims 20-34 are novel.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this Reply Brief, and any documents referred to as attached therein, are being facsimile transmitted on this date, February 19, 2003, to the U.S. Patent and Trademark Office, Washington, DC 20231.

Pam Turnbough

Date: February 19, 2003

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